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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/145,180	09/01/1998	JIA-HE LI	23356-M5	5665

7590 12/04/2001

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EXAMINER

WANG, SHENGJUN

ART UNIT	PAPER NUMBER
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1617

23

DATE MAILED: 12/04/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/145,180

Applicant(s)

LI ET AL.

Examiner

Shengjun Wang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 184-233 is/are pending in the application.
- 4a) Of the above claim(s) 193-195, 197-206, 208, 214, 215 and 217-233 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 184-192, 196, 207, 209-213 and 216 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 21, 22
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. The request filed on August 30, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/145180 is acceptable and a CPA has been established. An action on the CPA follows.

Applicants' election in the parent application is presumed to carry over to the instant CPA since applicants have not indicated a contrary intention.

Claims 184-233 are pending, claims 193-195, 197-206, 208, 214, 215 and 217-233 are withdrawn as drawn to nonelected species.

References No. 1-549 on CD presented in IDS paper No. 21 have not been considered because they are not legible copy to the examiner. See, 37 C.F.R. 1.98.

### *Claims Rejections 35 U.S.C. - 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 184-192, 196, 207, 209-213 and 216 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weltin et al. (AT of page 5, IDS paper No. 3) in view of Banasik et al. (AH, IDS paper No. 4), Suto et al (AR, IDS paper No. 4) and Endres et al. (AT of page 2, IDS paper No. 3).

Weltin et al. (AT of page 5, IDS paper No. 3) teach that 6(5H)-phenanthrindione, an isoquinoline derivative, is a potent inhibitor of poly(ADP-ribose) polymerase (PARP). See the abstract and Figure 1.

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Weltin et al. do not teach expressly the employment of a substituted 6(5H)-phenanthrindinone, i.e., 10-amino-2-nitro-6(5H)-phenanthrindinone, for treating ischemia.

However, Endres et. al. (AT of page 2, IDS paper No. 3) teach a method of treating ischemia by inhibition of PARP activity. See page 1144, third paragraph. Suto et al. (AR, IDS paper No. 4) teach a method of optimization of PARP inhibiting activity of isoquinoline derivatives. The method comprising adding various substituents, e.g., nitro and amino groups, to isoquinoline derivatives. Isoquinoline derivative with substituent at 5 position give optimal results. See, page 109, table 1. Banasik et al teaches that 2-nitro substituted 6(5H)-phenanthrindinone have more inhibition activity against PARP than 6(5H)-phenanthrindinone. ( $IC_{50}$  0.35  $\mu$ M). See page 1573 right column, compound No. 3.

Therefore it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ substituted 6(5H)-phenanthrindinone, e.g., 10-amino-2-nitro-6(5H)-phenanthrindinone for treating ischemia

A person of ordinary skill in the art would have been motivated to employ substituted 6(5H)-phenanthrindinone, e.g., 10-amino-2-nitro-6(5H)-phenanthrindinone for treating ischemia because 6(5H)-phenanthrindinone is a known potent PARP inhibitor and PARP inhibitors are known to be useful for treating ischemia disorder, a derivative of 6(5H)-phenanthrindinone is reasonably expected to be similar useful. Furthermore, since optimization of PARP inhibiting activity of isoquinoline derivatives by amino and/or nitro substituents is known in the art, a person with ordinary skill in the art would have been reasonably expected to optimize of PARP inhibiting activity of 6(5H)-phenanthrindinone by adding amino and/or nitro group to 6(5H)-phenanthrindinone. 10-amino-2-nitro-6(5H)-phenanthrindinone is seen as an obvious optimal

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variation of isoquinoline derivatives known as PARP inhibitors and such optimization is considered within the skill of artisan, absent evidence to the contrary. The additional amino substituent at 10 position is particular obvious because Suto teaches 5 amino substituted isoquinoline is particular active. (5 position in isoquinoline is corresponding to 10 position in 6(5H)-phenanthridinone. Finally, developing a method for administration is considered within the skill of artisan.

Applicants remarks submitted June 28, 2001 have been fully considered, but are not persuasive for reasons discussed below.

Applicants assert that the examiner has not indicated however, nor does the art describe, that substitutions made to dihydroisoquinolinone or an isoquinoline would have the same biological out come or effect as substitution made to a phenanthridinone. Applicant's assertion is correct. What the art described, which the examiner <sup>also</sup> ~~rely~~ on as base of obvious, is the teaching of how to optimize the activity of isoquinoline by substituting it with amino and or nitro group. As discussed above, such optimization is considered within the skill of artisan. The elected species is particular obvious over the cited prior art as discussed above. Further, Phenanthridinone is a derivative of isoquinoline not because Weltin say it is, phenanthridinone is a derivative of isoquinoline because it contain the isoquinoline moiety. Further, they are known to have the same biological property, i.e., inhibition of PARP.

The claimed inventions are seen to be obvious over the cited prior art for reasons discussed above, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (703) 308-4554. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Shengjun Wang

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November 30, 2001

RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200